Remarks

Claims 17, 37 and 35 have been cancelled by this amendment, as redundant. The claims have been amended to more precisely define the types of bicyclic ring system in the compounds. Claim 21 has been amended to specifically define the types of disorders to be treated by virtue of the specific neurotransmitters whose altered release characterizes the disorder.

Response to Restriction Requirement

In response to the Restriction Requirement, Claims 1, 21 and 41 have been amended to specify that the azabicyclic ring is a 7-membered ring, and either p or 1 is 1, as suggested by the Examiner.

Objection

Claims 2-6, 8-10, 20, 22-26, 28-30, 40, 48-50, and 60 were objected to as being of improper dependent form. The basis for the objection was that the 5 or 6 member aromatic rings in Claims 1, 21 and 41 did not specify that they were substituted, whereas the 5 or 6 member rings in the objected-to claims specified that the rings were substituted.

The term "aromatic ring" is well understood in the art to include any ring that is aromatic. The presence of substituents does not effect the aromaticity of the ring (i.e., whether or not the rings include subsituents has no bearing on whether they are aromatic rings, or whether they include 5 or 6 members in the rings). Those of skill in the art know what is meant by a 5 or 6 membered aromatic ring, and know that such rings can be substituted and still include 5 or 6 members in the ring itself, and still be aromatic.

However, to facilitate allowance, Applicants have amended the claims to state that the group Cy includes 5 or 6 member aromatic rings and 5 or 6 member substituted aromatic rings. That the rings can be substituted is clear from the specification and the claims as originally filed (i.e., the dependent claims specify that the Cy rings can be substituted). Accordingly, this amendment adds no new matter to the claims.

Rejection under 35 U.S.C. § 112, First Paragraph

Claim 21 was rejected under 35 U.S.C. § 112, first paragraph, as non-enabled. The basis for the rejection is that the claims are directed to a method for treating a disorder characterized by an alteration in normal neurotransmitter release, without specifically listing the neurotransmitters. Applicants have addressed this rejection by specifically referring to those neurotransmitters discussed in the specification on page 4, lines 1-5, namely, nicotinic cholinergic neurotransmitters. A simple search on Medline using the term "nicotinic cholinergic neurotransmitter" will identify thousands of research articles that identify disorders mediated by alteration in the normal release of nicotinic cholinergic neurotransmitters. Accordingly, this term is so well known to those of skill in the art that it is clear the amended claim is enabled.

Claims 1-7, 11-14, 18-27, 31-34, 38-47, 41-54 and 58-60 were rejected under 35 U.S.C. § 112, first paragraph, as including subject matter not described in the specification. Specifically, the Office Action stated that the phrase "B' is alkylenic" lacked descriptive support in the specification. To facilitate allowance, Applicants have deleted the phrase "B' is alkylenic" from the claims, as suggested by the Examiner, thus mooting this rejection. However, this term is present in the claims as originally filed, and thus is believed to have been adequately supported.

Rejection under 35 U.S.C. § 112, Second Paragraph

Claims 1-7 and 11-60 were rejected under 35 U.S.C. § 112, second paragraph, as indefinite.

Rejections related to the term "substituted"

The Office Action states that the term "substituted" in Claim 1 and elsewhere in the claims is indefinite. The claims have been amended to more particularly describe the types of substituents. Applicants have amended the claims to include language from page 8, lines 8-10, which describes the types of substituents that can be present on the "substituted" groups. Thus, the term "substituted" as applied to the terms "substituted alkyl, substituted alkenyl, substituted heterocyclyl, substituted cycloalkyl, substituted aryl, substituted alkylaryl, arylalkyl, and substituted arylalkyl refers to one or more alkyl, hydroxy, alkoxy, halo or amino substituents.

Rejections related to the term "alkylenic"

The Office Action further states that the term "B' is alkylenic" in Claim 1 and elsewhere in the claims is indefinite. The claims have been amended to delete reference to this term, thus mooting this rejection.

Rejections related to the term "acetylenic"

The Office Action also states that the term "acetylenic" in Claim 1 and elsewhere in the claims is indefinite. Acetylenic refers to -C≡C-, and for purposes of clarity, applicants have amended the claims to define acetylenic in this manner. This understanding of the term "acetylenic" is clear from its use in the context of the chemical formula in Claim 1. That is, there is no other possible definition of a two carbon bridging moiety that includes a triple bond, as there can only be four bonds on each carbon, and three of these four are taken up by the triple bond. Therefore, only one bond on each carbon is taken up with respect to the point of attachment to the remainder of the molecule. It is believed that the amendment and comments are both supported by the specification and moot the rejection.

Rejections related to the phrase "B' is a two carbon bridging species"

The Office Action still further states that the phrase "B' is a two carbon atom bridging species" in Claims 17, 37 and 57 is unclear. Applicants have amended the claims to delete reference to the alkylene bridging moieties, leaving only the ethylenic and acetylenic briding moieties. Accordingly, Claims 17, 37 and 57 no longer narrow the scope of the claims from which they depend and have been cancelled, thus mooting the rejection.

Rejections related to the phrase "Zj"

The Office Action has also stated that the use of j in both the upper and lower cases is inconsistent. This inconsistency has been fixed by amendment.

Rejections related to the phrase "alteration in normal neurotransmitter release"

The Office Action questioned which disorders are within the scope of Claim 21; that is, which disorders are characterized by an alteration in normal neurotransmitter release. Claim 21 has been amended to specify that the neurotransmitters are nicotinic cholinergic neurotransmitters. The specification provides sufficient detail to identify which disorders are covered by the amended claim (i.e., which are the result of an alteration in normal nicotinic cholinergic neurotransmitter release). Also, a simple search on Medline shows that it is well known which disorders are caused by this type of alteration of neurotransmitter release. As Applicants are not required to teach that which is well known, they respectfully request that this rejection be withdrawn.

The Office Action expressed some concern regarding the appropriate dosage regimen to treat the various disorders, and that pharmaceuticals might work with some patients and not others. Indeed, this type of question exists with virtually every pharmaceutical, which is why the United States Food and Drug Administration (USFDA) requires detailed clinical trials to address safety, efficacy, and dosage for each proposed treatment. Applicants respectfully assert that this line of inquiry is best suited for the USFDA, and not the USPTO. There is no requirement in U.S. patent law to have completed clinical trials suitable for FDA approval in order to obtain a U.S. patent. Substantial literature precedent exists that modulation of nicotinic cholinergic receptors is a useful therapeutic modality for treating disorders resulting from an alteration in normal neurotransmitter release, and no legitimate basis has been raised to doubt that this is true.

Indeed, it is believed that the majority of pharmaceutical companies would not spend the estimated hundreds of millions of dollars to pursue USFDA approval if they did not already have a U.S. patent in place, out of the fear that generic drug companies could immediately compete with them if the pharmaceutical, a composition including the pharmaceutical, or a method of treatment using the pharmaceutical, was not already covered by a U.S. patent. Accordingly, it is respectfully submitted that the claims as pending are fully enabled, and to hold otherwise would set a bad precedent for pharmaceutical discovery.

Before the method is actually practiced within the United States, the Examiner's concerns regarding how many patients will need to be tested, and other concerns raised, will undoubtedly

be addressed. It is respectfully believed that the amendment to Claim 21 (coupled with the wealth of knowledge in the relevant field), has adequately addressed this rejection, and respectfully request that it be withdrawn.

Conclusion

It is believed that the claims are currently in condition for allowance. The Examiner is encouraged to contact Applicants' undersigned representative if there any questions regarding the above.

Respectfully submitted,

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